Claims

Compounds of formula I

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$$(R_1)_g$$

$$A$$

$$B$$

$$R_4$$

$$R_3$$

including pharmaceutically acceptable salts thereof in which

A is methylene or -O-;

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B is methylene or -O-;

g is 0, 1, 2, 3 or 4;

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 R_1 represents a) halo, b) an alkyl group containing 1 to 3 carbon atoms optionally substituted by one or more halo, c) an alkoxy group containing 1 to 3 carbon atoms optionally substituted by one or more halo, d) an alkylthio group containing 1 to 3 carbon atoms optionally substituted by one or more halo, e) hydroxy, f) an acyloxy group containing 1 to 3 carbon atoms, g) hydroxymethyl, h) cyano, i) an alkanoyl group containing 1 to 6 carbon atoms, j) an alkoxycarbonyl group containing 2 to 6 carbon atoms, k) a carbamoyl group or carbamoylmethyl group each optionally N-substituted by one or two alkyl groups each containing 1 to 3 carbon atoms, l) a sulphamoyl or sulphamoylmethyl group each optionally N-substituted by one or two alkyl groups each containing 1 to 3 carbon atoms, m) an amino group optionally substituted by one or two alkyl groups each containing 1 to 3 carbon atoms; or two adjacent R_1 groups together with the carbon atoms to which they are attached form a fused benz ring, the substituents represented by R_1 being the same or different when g is 2, 3 or 4;

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R₂ is H, an alkyl group containing 1 to 3 carbon atoms, or an alkoxy group containing 1 to 3 carbon atoms;

 R_3 and R_4 , which are the same or different, are H, or an alkyl group containing 1 to 3 carbon atoms;

U is an alkylene chain containing 1 to 3 carbon atoms, optionally substituted by one or more alkyl groups each containing 1 to 3 carbon atoms;

Q represents a divalent group of formula IIa, IIb or IIc

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$$-N \stackrel{X}{\searrow} V \stackrel{R_5}{\longrightarrow} IIc$$

in which V is a bond or an alkylene chain containing 1 to 3 carbon atoms optionally substituted by one or more alkyl groups each containing 1 to 3 carbon atoms;

V' is an alkylene chain containing 2 to 6 carbon atoms, optionally substituted by one or more alkyl groups containing 1 to 3 carbon atoms;

X is an alkylene chain containing 0 to 2 carbon atoms and X' is an alkylene chain containing 1 to 4 carbon atoms provided that the total number of carbon atoms in X and X' amounts to 3 or 4;

R₅ is H or an alkyl group containing 1 to 3 carbon atoms; and

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T represents an aromatic group optionally containing one or more N atoms and optionally substituted by one or more substituents selected from halo, an alkyl

group containing 1 to 3 carbon atoms, an alkoxy group containing 1 to 3 carbon. atoms, or a polyhalogenated alkyl group, or T represents benzo[b]furanyl or benzodioxanyl with the proviso that T is not 2-pyrimidinyl when A is -O-; for use in reducing cravings to food or an addictive substance.

The use of compounds of formula I as claimed in claim 1 wherein A is -O-. **Z**.

3. The use of compounds of formula I as claimed in any preceding claim wherein R is -O-.

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The use of compounds of formula I as claimed in any preceding claim 4. wherein g is 0, 1 $\delta \tau$ 2.

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5. The use of compounds of formula I as claimed in any preceding claim wherein R₁ represents halò, an alkyl group containing 1 to 3 carbon atoms, an alkoxy group containing 1 to 3 carbon atoms, hydroxy, or two adjacent R₁ groups together with the carbon atoms to which they are attached form a fused benz ring.

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- 6. The use of compounds of formula I as claimed in any preceding claim wherein R₁ represents methoxy, fluoro, chloro, hydroxy, or two adjacent R₁ groups together with the carbon atoms to which they are attached form a fused benz ring.
- 7. The use of compounds of formula I as claimed in any preceding claim wherein R₂ is H or an alkyl group containing 1 to 3 carbon atoms.

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8. The use of compounds of formula I as claimed in any preceding claim wherein R₃ and R₄, which are the same or different, are H or methyl.

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- The use of compounds of formula I as claimed in any preceding claim 9. wherein T is pyridyl, pyrimidinyl, pyrazinyl, phenyl, benzofuryl, 1,4-benzodioxanyl or quinazolinyl all optionally substituted by methoxy, trifluoromethyl, or halo.
- 10.
- The use of compounds of formula I as claimed in any preceding blaim wherein T is 2-pyridyl, 2-pyrimidinyl, 2-pyrazinyl, phenyl, 2,3-dihydrobenzo[b]furan-X-

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- yl, 1,4-benzodioxan-5-yl or 4-quinazolinyl all optionally substituted by methoxy, trifluoromethyl, or halo.
- 11. The use of compounds of formula I as claimed in any preceding claim wherein R_5 is H or methyl.
 - 12. The use of compounds of formula I as claimed in claim 1 which are:
- N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(pyrazin-2-yl)piperid-4-yl]methylamine;
- 10 N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(3-chloropyrid-2-yl)pjperid-4-yl]methylamine;
- 15 <u>N</u>-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(quinazolin-4-yl)pjperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(pyrid-2-yl)piperid-4-yl]methylamine;
- N-(8-Methoxy-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4-20 yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-N'-[3-(trifluøromethyl)-2-pyridyl]ethanediamine;
- N-(8-Methoxy-1,2,3,4-tetrahydronaphth-2-ylmethyl)-1-[1-pyrimidin-2-yl)piperid-4yl]methylamine;
 - 7-{N-[1-(Pyrimidin-2-yl)piperid-4-ylmethyl]aminomethyl}-5,6,7,8-tetrahydronaphth-1-ol;
- 30 <u>N</u>-(5-Methoxy-3,4-dihydro-2<u>H</u>-1-benzopyran-3-ylmethyl)-1-[1-(pyrimidin-2-yl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-(1-phenylpiperid-4-yl)methylamine;
- 35 <u>N</u>-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(1,4-benzodioxan-5-yl)piperid-4-yl]methylamine;

propanediamine:

- 1-[1-(1,4-Benzodjóxan-2-ylmethyl)piperid-4-yl]-N-(2-methoxyphenyl)methylamine;
- 40 <u>N</u>-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(4-methoxyphenyl)piperid-4-yl]methylamine; <u>N</u>-(8-Methoxy-1,4-benzodioxan-2-ylmethyl)-<u>N</u>'-(2-methoxyphenyl)-1,3-
- 45 N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(3-methoxyphenyl)piperid-4-yl]methylamine;
 N-(6,7-Dichloro-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4-yl]methylamine;

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N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(2-chlorophenyl)piperid-4-yl]methylamine;

N-(\(\frac{5}{-Fluoro-1}, 4-\text{benzodioxan-2-ylmethyl})-1-[1-(2-\text{methoxyphenyl})\(\text{piperid-4-}\) yl]methylamine;

N-(8-Flàoro-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl]methylamine;

1-[1-(2-methoxyphenyl)piperid-4-yl]-N-(naphtho[1,2-b]dioxan-2-10 ylmethyl)methylamine;

1-[1-(2,3-Dihydròbenzo[b]furan-7-yl)piperid-4-yl]-N-(8-methoxy-1,4-benzodioxan-2ylmethyl)methylamine;

N-(6-Chloro-1,4-ben2odioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl]methylamine;

N-(7-Chloro-1,4-benzodio)an-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl]methylamine;

N-(8-hydroxy-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl]methylamine;

- □ 25 and pharmaceutically acceptable salts thereof in the form of individual enantiomers, racemates, or other mixtures of enantiomers.
 - The use of compounds of formula I as claimed in claim 12 which are:-13.
 - (S)-(-)-N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4-30 yl]methylamine;

(R)-(+)-N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl]methylamine;

(-)-N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(pyrid-2-yl)piperid-4-yl]methylamine dihvdrochloride:

(+)-N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(pyrid-2-yl)piperid-4\yl]methylamine dihydrochloride. 40

The use of compounds of formula I 14)

$$(R_1)_g \xrightarrow{A \xrightarrow{R_2} U - Q - T}$$

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and pharmaceutically acceptable salts thereof in the form of individual enantiomers? racemates, or other mixtures of enantiomers, in which

A is -O-;

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B is -O-;

g is 0 or 1;

R₁ represents halo, an alkyl group containing 1 to 3 carbon atoms, an alkoxy group containing 1 to 3 carbon atoms, or hydroxy;

 R_2 , R_3 and R_4 are each H;

15 U is methylene;

Q is a group of formula IIa or IIc

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$$-N \stackrel{X}{\underset{X'}{\longrightarrow}} V \stackrel{R_{5}}{\longrightarrow} N$$
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in which V is methylene or ethylene; X is an alkylene chain containing 0 to 2 carbon atoms and X'/is an alkylene chain containing 1 to 4 carbon atoms provided that the total number of carbon atoms in X and X' amounts to 3 or 4; and R5 is H; and

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is pyridyl, pyrazinyl, phenyl, benzo[b]furanyl, 1,4-benzodioxanyl, or quinazolinyl all optionally substituted by methoxy, trifluoromethyl, or halo; for use in réducing cravings to food or an addictive substance.

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- 15) The use of compounds of formula I as claimed in claim 14 wherein R₁ represents methoxy, fluoro, chloro or hydroxy.
- 16) The use of compounds of formula I as claimed in claim 14 wherein T is 2-pyridyl, 2-pyrazinyl, phenyl, 2,3-dihydrobenzo[b]furan-7-yl, 1,4-benzodioxan-5-yl or 4-quinazolinyl all optionally substituted by methoxy, trifluoromethyl, or halo.
 - 17) The use of compounds of formula I as claimed in claim 14 selected from:
- 10 N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(pyrazin-2-yl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(3-chloropyrd-2-yl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(quinazolin-4-yl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(pyrid-2-yl)piperid-4-yl]methylamine;
- 20 <u>N</u>-(8-Methoxy-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-(1-phenylpiperid-4-yl)methylamine;
- 25 N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(1,4-benzodioxan-5-yl)piperid-4-yl]methylamine;
 - 1-[1-(1,4-Benzodioxan-2-ylmethyl)piperid-4-yl]-N-(2-methoxyphenyl)methylamine;
 - 30 N-(1,4-Benzodioxan-2-yl/methyl)-1-[1-(4-methoxyphenyl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2/ylmethyl)-1-[1-(3-methoxyphenyl)piperid-4-yl]methylamine;
 - N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(2-chlorophenyl)piperid-4-yl]methylamine;
 - 35 N-(5-Fluoro-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4-yl]methylamine;
 - N-(8-Fluoro-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl]methylamine;
 - 1-[1-(2/,3-Dihydrobenzo[b]furan-7-yl)piperid-4-yl]-N-(8-methoxy-1,4-benzodioxan-2-ylmethyl)methylamine;
 - 45 N/(6-Chloro-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4-yl]methylamine;

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N-(7-Chloro-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl)methylamine;

N-(8-hydroxy-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl]methylamine;

and pharmaceutically acceptable salts thereof in the form of individual enantiomers, racemates, or other mixtures of enantiomers.

- 10 18) The use of compounds of formula I as claimed in claim 14 which are:-
 - (S)-(-)-N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(2-methoxyphenyl)piperid-4yl]methylamine;
- (R)-(+)-N-(1,4-Benzodioxan-2-ylmèthyl)-1-[1-(2-methoxyphenyl)piperid-4-15 yl]methylamine;
 - (-)-N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(pyrid-2-yl)piperid-4-yl]methylamine dihydrochloride;
 - (+)-N-(1,4-Benzodioxan-2-ylmethyl)-1-[1-(pyrid-2-yl)piperid-4-yl]methylamine dihydrochloride.
 - 19) The compound of formula I as claimed in claim 14 which is:
- 25 N-(7-Chloro-1,4-benzodioxan-2-ylmethyl)-1-[1-(2-methoxy)henyl)piperid-4yl]methylamine;

and pharmaceutically acceptable salts thereof in the form of individual enantiomers, racemates, or other mixtures of enantiomers.

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- The use of pharmaceutical compositions comprising a therapeutically effective amount of a compound of formula I, together with a pharmaceutically acceptable diluent or carrier in reducing cravings to food or an addictive substance
- 35 21. A method of reducing cravings to food or an addictive substance which comprises the administration of a therapeutically effective amount of a compound of formula I as claimed in any of claims 1 to 19 to a patient in need thereof.
- 22. A method as claimed in claim 15 wherein the addictive substance is cocaine, 40 amphetamine, nicotine, opiates, tobacco, alcohol or ecstasy.

The use of a compound of formula I as claimed in any of claims 1 to 19 in the manufacture of a medicament for use in reducing cravings to food or an addictive --substance.